

## WE CLAIM:

1. An apparatus for ionizing at least one analyte in a sample for delivery to a mass analysis device, comprising:

5 (a) an ionization enclosure including a passageway configured for delivery of ions to the mass analysis device;

(b) means to maintain said ionization enclosure at an ambient pressure of greater than 100 mTorr;

(c) a holder configured for maintaining a matrix containing said sample in said ionization enclosure at said ambient pressure;

10 (d) a source of laser energy including means associated with said ionization enclosure for directing the laser energy onto said matrix maintained by said holder at said ambient pressure to desorb and ionize at least a portion of said analyte in the sample, and

(e) means for directing at least a portion of said at least one ionized analyte into said passageway.

15 2. The apparatus of claim 1 wherein said at least one analyte in a matrix is located on a surface; on or in one or more wells of a multi-well microtitre plate; a microchip array; on or from a thin layer chromatographic plate; on, in or from an electrophoresis gel, on or from a membrane, or combinations thereof.

20 3. The apparatus of claim 1 wherein the sample holding means is any conventional single or multi-chambered containment article.

4. The apparatus of claim 1 wherein the sampling occurs using a static or a flowing liquid sample.

5. The apparatus of claim 1 wherein the mass analysis device is a mass spectrometer;

25 6. The apparatus of claim 1 wherein the source of laser energy is selected from a laser operated at ultraviolet (UV), visible (VIS) or infrared (IR) wavelengths or combinations thereof.

7. The apparatus of claim 1 wherein the ambient pressure is atmospheric pressure.

30 8. An apparatus for mass analysis of at least one analyte in a sample, comprising:

(a) an ion source having an ionization enclosure and a mass analysis device having a mass analysis enclosure, said ionization enclosure being connected with said mass analysis enclosure through a passageway configured for delivery of ions from the ion source to the mass analysis device, said ion source including:

5 (1) a holder configured for maintaining a matrix containing a sample in the ionization enclosure at ambient pressure;

(2) means associated with said ionization enclosure for directing energy from a laser onto a matrix maintained by said holder at ambient pressure to desorb and ionize at least a portion of said at least one analyte in the sample, and

10 (3) means for directing at least a portion of said ionized analyte into said passageway; and

(b) means to maintain said ionization enclosure at an ambient pressure greater than 100 mTorr while maintaining said mass analysis enclosure at a pressure less than about  $10^{-5}$  Torr.

15 9. The apparatus of claim 8 wherein the mass spectrometric analyzer is selected from time-of-flight, ion trap, quadrupole, Fourier transform ion cyclotron resonance, magnetic sector, electric sector, or combinations thereof.

10. The apparatus of claim 8 wherein the laser is operated at ultraviolet (UV), visible (VIS), or infrared (IR) wavelengths or combinations thereof.

20 11. The apparatus of claim 8 wherein said at least one analyte in a matrix is located on a surface; on or in one or more wells of a multi-well microtitre plate; a microchip array; on or from a thin layer chromatographic plate; on, in or from an electrophoresis gel, on or from a membrane, or combinations thereof;

25 wherein the sample holding means is any conventional single or multi-chambered containment article; or

the sampling occurs using a static or a flowing liquid sample.

12. The apparatus of claim 8 wherein in step (a), the operation of the MALDI configuration and sampling occurs in air, helium, nitrogen, argon, oxygen, carbon dioxide, or combinations thereof.

30 13. The apparatus of claim 8 wherein the source of laser energy is selected from a laser operated at ultraviolet (UV), visible (VIS) or (IR) infrared wavelengths or

combinations thereof, and the laser is stationary.

14. The apparatus of claim 8 wherein the ambient pressure is atmospheric pressure.

15. A method for preparing for mass analysis a sample that may contain at least one analyte, comprising:

(a) providing a matrix containing said sample; and

(b) maintaining the said matrix containing said sample in a condition of ambient pressure greater than 100 mTorr while directing laser energy onto the matrix to desorb and ionize at least a portion of the at least one analyte, and

(c) directing at least a portion of the ionized at least one analyte into a mass analysis device.

16. The method of claim 15 wherein the MALDI is operated at or near ambient pressure and the sample is maintained in a cooled or heated state from between about -196 to 500 °C.

17. The method of claim 15 wherein at least one analyte is an organic compound selected from small molecules having a molecular weight of less than about 1000 daltons and synthetic organic polymers having a molecular weight of up to 1,000,000 daltons, or fragments of these compounds or polymers.

18. The method of claim 15 wherein at least one analyte is a biologically related or biologically derived material selected from the group consisting of deoxyribonucleic acid (DNA), ribonucleic acid (RNA), peptide, protein, lipid, carbohydrate, an organism, a plasmid, bacteria, fungi, algae, viral particles, cells and combinations and fragments thereof.

19. The apparatus of claim 15 wherein the source of laser energy is selected from a laser operated at ultraviolet (UV), visible (VIS) or (IR) infrared wavelengths or combinations thereof.

20. The apparatus of claim 15 wherein the ambient pressure is atmospheric pressure.

21. A method for analyzing a sample that may contain at least one analyte comprising:

(a) providing a matrix containing the sample;

(b) maintaining said sample matrix in a condition of ambient pressure greater than

100 mTorr while directing laser energy onto the matrix to desorb and ionize at least a portion of the at least one analyte;

(c) directing at least a portion of the ionized at least one analyte into a mass analysis device, and

5 (d) mass analyzing the portion of the at least one analyte that is received by the mass analysis device.

22. The method of claim 21 wherein the mass analysis device means is selected from the group consisting of time-of-flight, ion trap, quadrupole, Fourier transform ion cyclotron resonance, magnetic sector, electric sector, and combinations thereof.

10 23. The method of claim 21 wherein the laser is stationary and said at least one sample are multiple samples and the multiple samples are positioned and sequentially analyzed in an organized or a random manner.

24. The method of claim 21 wherein said at least one sample are multiple samples and are contained in a multiple sample holder which is stationary and said laser is mobile and is positioned to sequentially analyze the stationary multiple samples in an  
15 organized or random manner.

25. The method of claim 21 wherein the laser is operated at ultraviolet (UV), visible (VIS), or infrared (IR) wavelengths or combinations thereof.

26. The method of claim 21 wherein the operation of the apparatus sampling  
20 occurs in air, helium, nitrogen, argon, oxygen, carbon dioxide or combinations thereof.

27. The method of claim 21 wherein the sampling occurs in an inert environment selected from helium, nitrogen, argon or combinations thereof.

28. The method of claim 21 wherein the apparatus is operated at or near ambient pressure and the at least one sample is maintained at between about -196 to 500 °C.

25 29. The method of claim 21 wherein positive ions and negative ions are produced and analyzed.

30. The apparatus of claim 1 wherein said apparatus is maintained at a temperature between about -20° C and +100°C.

31. The apparatus of claim 1 wherein the pressure of the apparatus is maintained  
30 between about +15% and -15% of atmospheric pressure.

32. A method for the mass spectrometric analysis of ions produced by matrix-

assisted laser desorption and ionization of at least one analyte in a sample, wherein the improvement comprises conducting the matrix-assisted desorption and ionization at an ambient pressure greater than 100 mTorr.

- 5 33. Mass analysis apparatus including a matrix-assisted laser desorption and ionization (MALDI) source and a mass analysis device that receives and analyzes ions from the MALDI source, wherein the improvement comprises means for maintaining the MALDI source at an ambient pressure greater than 100 mTorr during the ionization and analysis.